THE ACTION OF ADRENALIN ON THE INTERNAL CAROTID AND VERTEBRAL ARTERIES

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny
Vol. 49, No. 5, pp. 10-15, May, 1960
Original article submitted April 18, 1959

By studying several indices of cerebral circulation we have been able to show [3] that the internal carotid and vertebral arteries play an important part in compensating for disturbances of the cerebral circulation resulting from interference with the outflow of blood from the brain. By fixing the arteries in vivo we were also able to reveal in which parts the "closure mechanisms" which control the flow of blood to the brain were localized. After further work we concluded that the simplest and most convenient way of determining the condition of these arteries was to determine directly the pressure drop (resistance) in them, because it is known that this quantity depends chiefly upon the size of the lumen; when the vessel is contricted the resistance increases, and vice versa. By measuring the pressure at both ends of the arteries, the aperture of the lumen may be determined.

In the present work we have studied the effect of adrenalin on the internal carotid and vertebral arteries. This action is important because adrenalin is one of the most widespread physiologically active substances and is concerned in the regulation of many functions including blood circulation. In addition, adrenalin or compounds closely related to it mediate the transmission of sympathetic nervous impulses, and our study may help to determine the effect of the sympathetic nervous system on the arteries supplying the brain.

METHOD

The experiments were performed at operation upon 13 adult rabbits. In some experiments the anesthetic used was chloral hydrate (0.4 g/kg), and in others urethane (1 g/kg). After operation, 0.3-0.4 ml/kg heparin was injected.

To determine changes in the size of the lumen, simultaneous recordings were made of the blood pressure in the aorta and in its major branches from which the vertebral and internal carotid arteries originate, and also in the circle of Willis, where they end. For this purpose it was necessary to ligature one of the carotid arteries, a procedure which does not affect the cerebral circulation [5]. A cannula was inserted in the direction of the thorax into the common carotid artery, and the pressure in the aorta and its major branches was recorded on a mercury manometer. A second cannula inserted into the same carotid artery in a cranial direction enabled the pressure in the circle of Willis to be recorded by the method previously described by Hürthle [6] and Opdyke [7] and Avrorov [1]. To increase the accuracy, we tied off all the branches of the artery being investigated except for the internal carotid, which was dissected out up to the point at which it enters the skull, and this artery was then effectively a continuation of the cannula and connected it directly with the circle of Willis. Before the experiment, both manometers were arranged so that their zero points were at the same level.

In some experiments, a compensator was used which enabled the aortic pressure to be maintained at a constant level. It consisted (Fig. 1) of a manometer, an air reservoir, and a vessel containing a blood substitute * which was connected by a wide cannula to the abdominal aorta below the renal arteries. In the compensator, the pressure was maintained at the same level as in the aorta. The compensator automatically corrected for any increase or decrease in arterial pressure.

RESULTS

It is known that even quite small doses of adrenalin cause an increase in arterial pressure. It is difficult to determine what effect it has on the circulation of the brain as a whole, and on the flow through the carotid and vertebral arteries in particular, because any increase in arterial pressure will have a marked influence on the arteries of the brain. It is therefore not possible to determine whether changes in the cerebral circulation are caused by the direct action of adrenalin on the arteries or whether they are the result of increased arterial pressure. On this account we maintained the arterial pressure at a constant level by means of the compensator, as has been described by Carlyle and Grayson [5], and by Thuranszky [8].

* The most suitable fluid was polyglucin, which has no antigenic properties.

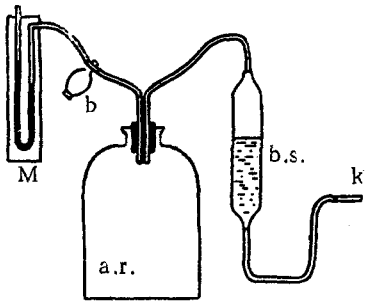

Fig. 1. Diagram of the compensator used to maintain arterial pressure. k) Cannulainserted into large artery and directed towards the heart; b.s.) blood substitute; a.r.) air reservoir; b) bulb with valve; M) manometer for measuring the pressure in the whole system.

When adrenalin is injected subcutaneously, it is absorbed slowly and at a rate which will depend upon the conditions. However, an intravenous injection will cause the pressure to rise so rapidly that it cannot be annulled by the compensator. We therefore injected $1 \cdot 10^{-4}$ adrenalin slowly into the peritoneal cavity. This enabled a comparatively slow increase of adrenalin in the blood to occur, and at the same time the compensator was effective in maintaining the arterial pressure constant.

The results of one experiment are shown in Fig. 2. In spite of the fact that there was no change in aortic pressure during the injection (upper curve), the pressure in the circle of Willis fell considerably (lower curve). This constitutes a direct demonstration of the increase in resistance offered by the internal carotid and vertebral arteries. Because there is no reason to expect any changes in blood viscosity, the effect observed can result only from the constriction of these arteries under the influence of adrenaline. The pressure between the two ends of these vessels, which indicates the increased resistance, was approximately doubled (Fig. 2, shaded area). The constrictor effect of adrenalin on these arteries is quite specific, because in our experiments it was eliminated by the adrenolytic substance dibenamine (TS-224).

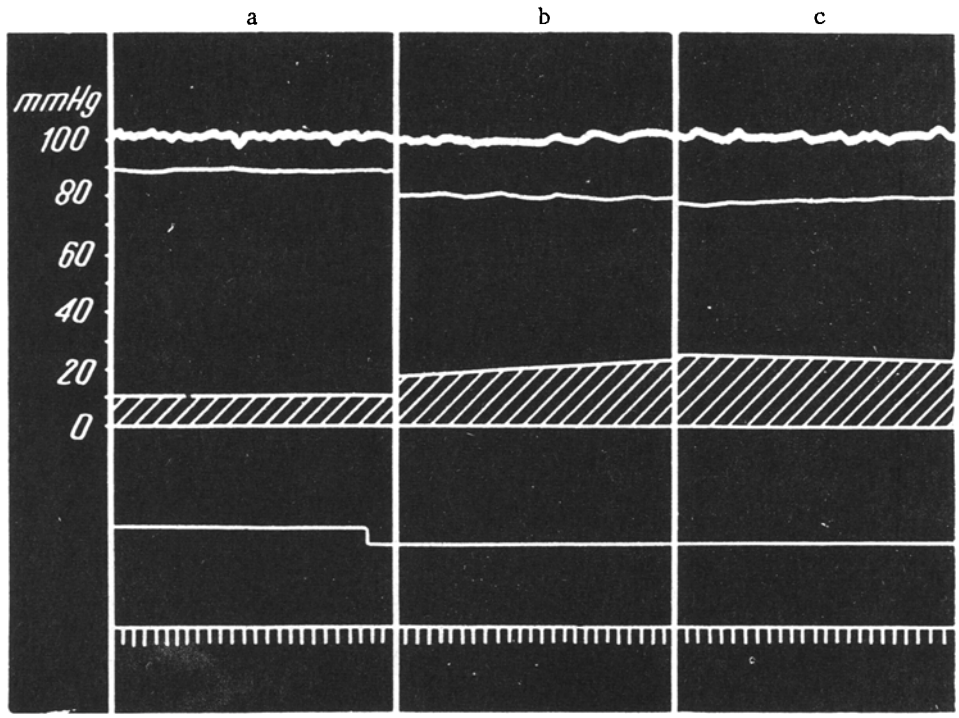

Fig. 2. Increase in the resistance of the internal carotid and vertebral arteries following slow intraperitoneal injection of $1: 10^{-4}$ adrenalin. Compensator used for arterial pressure. Upper curve –pressure in aorta; lower curve– pressure in circle of Willis; shaded area over the base line represents the difference of the two pressures and represents the resistance in the internal carotid and vertebral arteries; time marker–5 sec; a) Before the injection; b) ten minutes after the beginning of the injection, 18 min after beginning the adrenalin injection.

The action of adrenalin on the internal carotid and vertebral arteries was also observed after giving small repeated intravenous injections. The results of one such experiment are shown in Fig. 3. The elevation of arterial pressure (upper curve) was approximately the same for each adrenalin injection. However, if at the first injection the pressure in the circle of Willis (lower curve) increased beyond a certain level, then the second elevation was less well shown, and subsequently scarcely occurred at all. Such an increase in the difference between the pressures at the beginning and end of the arteries indicates their constriction. Therefore, to demonstrate the action of adrenalin on the internal carotid and vertebral arteries, either a larger dose or a longer time of action of adrenalin, is required. At the end of the experiment, as a control, a rather greater amount of adrenaline was injected, and this caused a greater increase in general arterial pressure and in the circle of Willis than previously.

Hürthle [6] was the first to make simultaneous measurements of the pressure in the aorta (m_1) and in the circle of Willis (m_2) and he thought that from the ratio $m_2/m_1 = \omega$ it would be possible to determine the condition of the arteries supplying the brain. His method is based on a model consisting of a right-angled triangle where one of the sides enclosing the right angle represents the vertical manometer tubes, and the hypotenuse represents the pressure gradient in a horizontal tube which forms the other side enclosing the right angle. The ratio m_2/m_1 then represents the resistance in the horizontal tube only in the case when there is a linear pressure gradient, which however is not the case in a vascular system. Hürthle himself [6] admitted that the method could be applied to the blood system of the brain only under the conditions that the resistance in the blood vessel connecting the manometers (i.e., in the arteries supplying the brain) remained constant: actually, however, the lumen of these vessels and of all their branches may undergo considerable changes.†

It is quite evident that the readings of two manometers placed at different points of the vessels can indicate only the resistance between them, so that the resistance would be represented by the difference in

† Hürthle's method has not been in common use for 70 years, and we would not have discussed it had not V. P. Avrorov [2] used it to explain his experimental results.

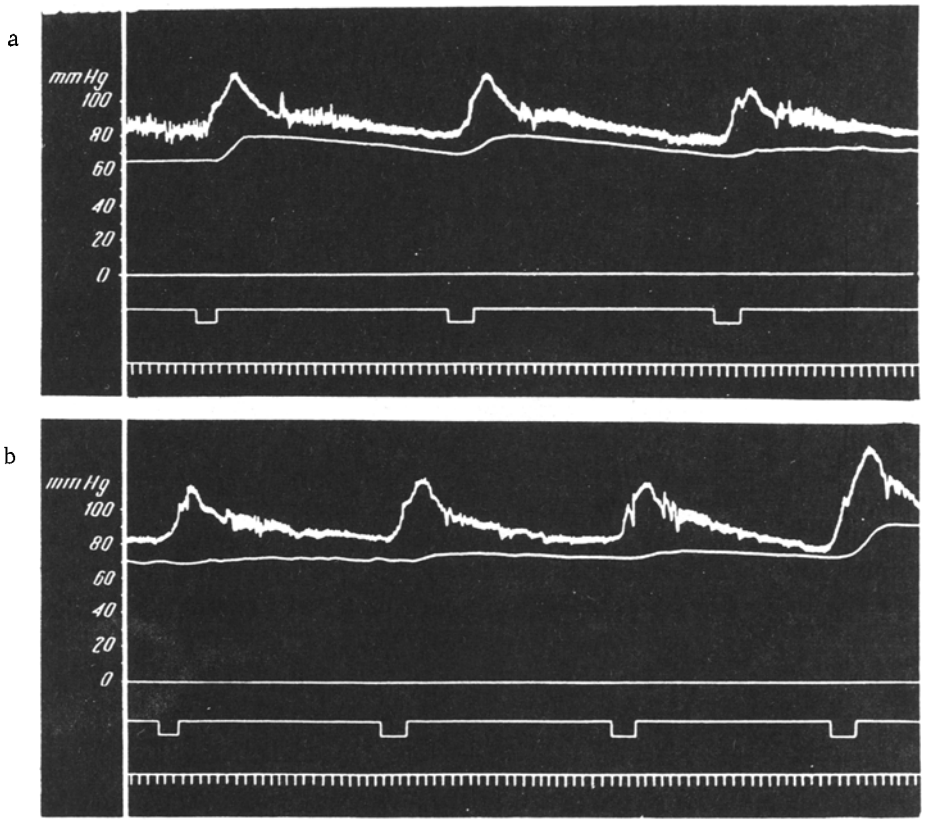

Fig. 3. Increase in the resistance of the internal carotid and vertebral arteries following repeated intravenous injections of 0.1 ml 1 : 10^{-4} adrenalin; the seventh injection is of 0.2 ml. Upper curve) pressure in aorta; next curve) pressure in the circle of Willis, then follow : zero line, marker indicating adrenalin injection, 5 sec time marker; b represents a direct continuation of trace a. Explanation in text.

pressure and not, as proposed by Hürthle, by the ratio m_2/m_1. If deductions are to be made from this ratio, then the results shown in Fig. 2 would have to be interpreted as indicating an expansion of the blood vessels. However, our direct measurements showed this conclusion to be erroneous , because micrographs of the pial vessels and measurement of their diameter on the film made with a micrometer microscope eyepiece showed that not only did the superficial arteries not expand , but that they were actually constricted by 4-5 %. At the same time the pressure in the venous sinuses of the brain fell somewhat.

The results of the present experiments allow the value of the resistance in the internal carotid and vertebral arteries to be determined. Under normal conditions (without adrenalin) the pressure drop represents approximately 12 % of the aortic pressure, and when adrenalin is injected the figure is 26 %, i.e., more than one quarter of the aortic pressure. These arteries may therefore represent a considerable resistance to cerebral blood flow, and this resistance is increased by adrenalin. The effect of adrenalin on the internal carotid and vertebral arteries, which we have shown to affect the blood flow to the circle of Willis, explains,on the one hand,certain aspects of the action of this physiologically active substance on the cerebral circulation, and,on the other hand,affords (admittedly indirect) evidence that the lumen of these arteries is under sympathetic control. The second point awaits direct experimental confirmation.

SUMMARY

Experiments were performed on rabbits. Measurements were made of the difference in pressure between the aorta and the circle of Willis, and the resistance of the internal carotid and vertebral arteries deduced. When the arterial blood pressure was stabilized by means of a compensator, it was shown that slow intraperitoneal injection of adrenalin caused a considerable constriction of these arteries. A similar reaction occurred following multiple intravenous adrenalin injections, and the pressure in the circle of Willis failed to follow the rise in aortic pressure.

It was shown that adrenalin injection caused a significant increase in the resistance of the internal carotid and vertebral arteries.

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‡ Original Russian pagination See C.B. Translation.